

melanoma cells in 50% Matrigel. Tumors were grown to a mean of $\sim 200 \text{ mm}^3$, at which point mice were grouped and dosing was initiated. Mice were dosed once daily by oral gavage with vehicle (20% 2-Hydroxypropyl- β -Cyclodextrin) or increasing doses of Compound C. Tumor volumes and body weights were measured over the course of 3 weeks, and doses were adjusted by body weight to achieve the proper dose in terms of mg/kg. At this time, animals were sacrificed, and tumors were dissected and imaged.

[0231] Results: As shown in FIG. 11 and FIG. 12, treatment with Compound C led to tumor growth inhibition in a dose-dependent manner with tumor regression observed at the highest (50 mg/kg) dose. As shown in FIG. 13, all treatments were well tolerated with no body weight loss observed (FIG. 13).

Example 17. Effects of BRG1/BRM ATPase Inhibition on the Growth of Uveal Melanoma and Hematological Cancer Cell Lines

[0232] Procedure: Uveal melanoma cell lines (92-1, MEL202, MP41, MP38, MP46), prostate cancer cells (22RV1), acute leukemia cells (EOL1, THP1), and histiocytic lymphoma cells (U937) were plated into 96 well plates with growth media (see Table 2). BRG1/BRM ATPase inhibitor, N—((S)-1-((4-(6-(cis-2,6-dimethylmorpholino)pyridin-2-yl)thiazol-2-yl)amino)-3-methoxy-1-oxopropan-2-yl)-1-(methylsulfonyl)-1H-pyrrole-3-carboxamide, was dissolved in DMSO and added to the cells in a concentration gradient from 0 to $2 \mu\text{M}$ (for uveal melanoma cell lines), or 0 to $1 \mu\text{M}$ (for other cell lines), at the time of plating. Cells were incubated at 37°C . for 3 days. After three days of treatment, cell growth was measured with Cell-titer glow (Promega), and luminescence was read on an Envision plate reader (Perkin Elmer).

[0233] Results: As shown in FIG. 14, N—((S)-1-((4-(6-(cis-2,6-dimethylmorpholino)pyridin-2-yl)thiazol-2-yl)amino)-3-methoxy-1-oxopropan-2-yl)-1-(methylsulfonyl)-1H-pyrrole-3-carboxamide resulted in potent growth inhibition in all the cell lines. As shown in Table 3, measured absolute IC_{50} values were below 350 nanomolar for all cell lines tested.

[0234] Table 3 lists the tested cell lines, growth media used, and absolute IC_{50} values (nM) after 3 days of compound treatment.

TABLE 3

Cell Lines, Growth Media, and Absolute IC_{50} values				
Cell Line	Source	Growth Media	Cancer Type	Absolute IC_{50} (nM)
22RV1	ATCC	RPMI1640 + 10% FBS	Prostate	29.7
92-1	SIGMA	RPMI1640 + 10% FBS	Uveal melanoma	0.3
EOL1	DSMZ	RPMI1640 + 10% FBS	Acute myeloid leukemia	75.5
MEL202	SIGMA	RPMI1640 + 10% FBS	Uveal melanoma	62.3
MP38	ATCC	RPMI1640 + 20% FBS	Uveal melanoma	31.5
MP41	ATCC	RPMI1640 + 20% FBS	Uveal melanoma	11.8
MP46	ATCC	RPMI1640 + 20% FBS	Uveal melanoma	112.6

TABLE 3-continued

Cell Lines, Growth Media, and Absolute IC_{50} values				
Cell Line	Source	Growth Media	Cancer Type	Absolute IC_{50} (nM)
THP1	ATCC	RPMI1640 + 10% FBS	Acute monocytic leukemia	344.9
U937	ATCC	RPMI1640 + 10% FBS	Histiocytic lymphoma	14.8

Example 18. BRG1/BRM ATPase Inhibition Causes Uveal Melanoma Tumor Growth Inhibition In Vivo

[0235] Procedure: Nude mice (Envigo) were engrafted subcutaneously in the axillary region with 5×10^6 92-1 uveal melanoma cells in 50% Matrigel. Tumors were grown to a mean of $\sim 200 \text{ mm}^3$, at which point mice were grouped and dosing was initiated. Mice were dosed once daily by oral gavage with vehicle (20% 2-Hydroxypropyl- β -Cyclodextrin) or increasing doses of N—((S)-1-((4-(6-(cis-2,6-dimethylmorpholino)pyridin-2-yl)thiazol-2-yl)amino)-3-methoxy-1-oxopropan-2-yl)-1-(methylsulfonyl)-1H-pyrrole-3-carboxamide. Tumor volumes and body weights were measured over the course of 3 weeks, and doses were adjusted by body weight to achieve the proper dose in terms of mg/kg.

[0236] Results: As shown in FIG. 15, treatment with N—((S)-1-((4-(6-(cis-2,6-dimethylmorpholino)pyridin-2-yl)thiazol-2-yl)amino)-3-methoxy-1-oxopropan-2-yl)-1-(methylsulfonyl)-1H-pyrrole-3-carboxamide led to tumor growth inhibition in a dose-dependent manner with tumor regression observed at the highest (1.5 mg/kg) dose. As shown in FIG. 16, all treatments were well tolerated based on % body weight change observed.

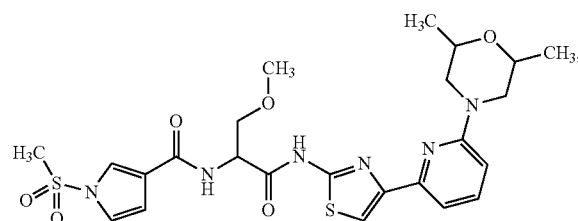
OTHER EMBODIMENTS

[0237] While the invention has been described in connection with specific embodiments thereof, it will be understood that invention is capable of further modifications and this application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure that come within known or customary practice within the art to which the invention pertains and may be applied to the essential features hereinbefore set forth, and follows in the scope of the claims.

[0238] Other embodiments are in the claims.

What is claimed is:

1. A compound having the structure:



or a pharmaceutically acceptable salt thereof.